

WHAT IS CLAIMED IS:

1. A method for identifying candidate substances that change the levels of accumulation of a protein comprising:

- 5 a) obtaining a cell expressing a chimeric polypeptide comprising a polypeptide region of the protein linked to at least one marker gene product region;
- b) exposing the cell to a candidate substance; and
- c) determining any change in a level of the chimeric protein subsequent to
- 10 exposing the cell with the candidate substance.

2. The method of claim 1, further comprising assaying the level of the chimeric protein using the marker gene product.

15 3. The method of claim 1, wherein the protein is an unstable protein.

4. The method of claim 3, wherein the unstable protein is a presenilin protein, an amyloid precursor protein, or an amyloid precursor protein derivative.

20 5. The method of claim 3, wherein the unstable protein is a presenilin protein.

6. The method of claim 5, wherein the presenilin protein is PS1.

7. The method of claim 5, wherein the presenilin protein is PS2.

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8. The method of claim 1, wherein the protein is further defined as a polytopic membrane protein.

9. The method of claim 9, wherein the polytopic protein further comprises at least

30 one co-factor.

10. The method of claim 9, wherein the polytopic protein is a ligand-gated ion channel or a voltage-gated ion channel.

5 11. The method of claim 10, wherein the polytopic protein is a ligand-gated ion channel and is further defined as a nicotinic acetylcholine receptor, a GABA receptor, or a glycine receptor.

10 12. The method of claim 10, wherein the polytopic protein is a voltage-gated ion channel and is further defined as a voltage-gated Na^{2+} channel, a voltage-gated K^{+} channel, or a voltage-gated Ca^{2+} channel.

13. The method of claim 1, wherein the change is an increase in the level of accumulation of said protein.

15 14. The method of claim 1, wherein the change is a decrease in the level of accumulation of said protein.

15. The method of claim 1, wherein the candidate substance is a chemical compound.

20 16. The method of claim 1, wherein the candidate substance is a protein.

17. The method of claim 16, further comprising isolation of the protein candidate substance.

25 18. The method of claim 1, wherein the candidate substance is a pharmacological compound.

19. The method of claim 1, wherein the candidate substance is a nucleic acid.

30 20. The method of claim 19, further defined as comprising transfecting the cell with the nucleic acid.

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21. The method of claim 19, wherein the nucleic acid is a cDNA.

22. The method of claim 19, wherein the nucleic acid is a genomic DNA.

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23. The method of claim 1, further defined as comprising contacting the cell with said candidate substance.

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24. The method of claim 1, further defined as comprising injecting the cell with the candidate substance.

25. The method of claim 1, further defined as comprising administering the candidate substance to the cell.

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26. The method of claim 1, wherein the marker gene product is an fluorescent gene product.

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27. The method of claim 26, wherein the fluorescent gene product is a yellow fluorescent protein (YFP), a green fluorescent protein (GFP), a blue fluorescent protein (BFP), or a red fluorescent protein (RFP).

28. The method of claim 1, wherein the marker gene product is an antibiotic resistance gene product.

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29. The method of claim 28, wherein the antibiotic resistance gene product is further defined as one that confers antibiotic resistance by binding stoichiometrically to an antibiotic.

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30. The method of claim 29, wherein the antibiotic resistance gene product is selected from the group consisting of a bleomycin resistance gene product, a zeocin resistance gene product, a zorbamycine resistance gene product, a victomycin resistance gene

product, a platomycin resistance gene product, a tallysomycin resistance gene product, a SF 1771 resistance gene product, a SF 1961 resistance gene product, and a YA 56 resistance gene product.

5 31. The method of claim 29, wherein the antibiotic resistance gene product is the bleomycin resistance gene product.

32. The method of claim 29, wherein the antibiotic resistance gene is the zeocin resistance gene.

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33. The method of claim 29, wherein the determining comprises an antibiotic selection assay.

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15 34. The method of claim 33, wherein the antibiotic selection assay comprises selection with a higher concentration of the antibiotic.

35. A method for identifying candidate substances that change the levels of accumulation of an unstable protein comprising

- 20 a) obtaining a cell expressing a chimeric polypeptide comprising a polypeptide of the unstable protein linked to at least one marker gene product;
- b) exposing the cell to a candidate substance; and
- c) determining any change in a level of the chimeric protein subsequent to exposing the cell with the candidate substance.

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36. The method of claim 35, further comprising assaying the level of the chimeric protein using the marker gene product.

37. The method of claim 35, wherein the protein is a presenilin protein.

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38. The method of claim 35, wherein the marker gene product is an antibiotic resistance gene product.

39. The method of claim 38, wherein the antibiotic resistance gene product is a bleomycin resistance gene product.

40. The method of claim 39, wherein the bleomycin resistance gene product is the Ble protein.

41. The method of claim 35, wherein the marker gene product is an green fluorescent gene product, a yellow fluorescent gene product, a blue fluorescent gene product, or a red fluorescent gene product.

42. The method of claim 41, wherein said determining measures the level of the green fluorescent gene product, the yellow fluorescent gene product, the blue fluorescent gene product or the red fluorescent gene product.

43. A method for identifying candidate substances that change the levels of accumulation of a presenilin protein comprising

- a) obtaining a cell expressing a chimeric presenilin polypeptide comprising a presenilin polypeptide linked to a bleomycin resistance gene product;
- b) exposing the cell to a candidate substance; and
- c) determining any change in a level of the chimeric presenilin subsequent to exposing the cell with the candidate substance.

44. The method of claim 43, wherein the chimeric polypeptide further comprises a fluorescent protein.

45. The method of claim 44, wherein the determining comprises measuring fluorescence.

46. The method of claim 43, wherein the determining comprises an antibiotic selection assay.

47. The method of claim 46, wherein the antibiotic is bleomycin.

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48. The method of claim 46, wherein the antibiotic selection assay is performed at a higher level of the antibiotic.

49. A method for identifying candidate substances that change the levels of accumulation of a presenilin protein comprising:

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- a) obtaining a cell expressing a chimeric presenilin polypeptide comprising a presenilin polypeptide linked to a fluorescent protein gene product;
- b) exposing the cell to a candidate substance; and
- c) determining any change in a level of the chimeric presenilin subsequent to exposing the cell with the candidate substance.

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50. The method of claim 49, wherein the fluorescent protein gene product is a green fluorescent gene product.

51. The method of claim 49, wherein the fluorescent protein gene product is a yellow fluorescent gene product.

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